Remarks

The title of the application has been amended. No amendments have been made to the claims.

1. **Technically Related U.S. Patents and Applications**

Applicants would like to bring to the Examiner's attention the following technically related U.S. patents and U.S. patent application. U.S. Patent Nos. 5,795,885 and 5,792,635 and U.S. Patent Application No. 10/824,661 are listed on a PTO-1449 form in the concurrently filed IDS under 37 C.F.R. 1.97(c). U.S. Patent No. 6,962,909 has been previously cited by the Examiner on a PTO-892 form.

Application No.	Earliest Effective Filing Date	Patent No.	Issue Date
08/483,057	June 7, 1995	5,795,885	August 18, 1998
08/474,799	June 7, 1995	5,792,635	August 11, 1998
09/985,417	June 7, 1995	6,962,909	November 8, 2005
11/376,117	June 7, 1995	--	--

An outstanding final office action has been issued by the Examiner in copending Application No. 11/376,117.

2. **Confirmation of Election of Invention**

Applicants confirm the election with traverse of the invention of Group IV (claims 26 to 32), drawn to a method of treating neovascularization in a mammal by squalamine. Accordingly, claim 25 has been withdrawn as directed to a non-elected invention.

3. **Information Disclosure Statement**

Applicants bring to the Examiner's attention that an Information Disclosure Statement has been concurrently filed with this response.

4. Rejection under 35 U.S.C. 112, first paragraph

The Examiner asserts that Applicants have "no possession of the invention of the subject matter as claimed at the time of filing the application." More specifically, the Examiner indicates that there is "no written description for a method of treating neovascularization in a mammal by using squalamine" or of treating rheumatoid arthritis in a human by using squalamine. In support of these assertions, the Examiner reproduces in the Office Action selected sections of MPEP 2163.06.

Applicants respectfully submit that claims 26 to 32 are fully supported by the specification based at least on the teaching by Applicants of (1) squalamine as being a potent inhibitor of neovascularization and (2) rheumatoid arthritis as being a disease state that would be readily treated by an inhibitor of neovascularization.

In pointing to evidence in Applicants' specification regarding the teaching of squalamine as a potent inhibitor of neovascularization, Applicants bring to the Examiner's attention the following representative sections

Paragraphs [0243] and [0244] of the published application describe the inhibition by squalamine of the growth of bovine pulmonary artery endothelial cells (BPE) *in vitro*.

Paragraphs [0245] through [0248] of the published application describe the inhibition by squalamine of human endothelial cell cord formation *in vitro*.

Paragraphs [0256] through [0260] describe that in the classical and widely accepted chorioallantoic membrane model assay, squalamine is an inhibitor of capillary growth, compatible with suppression of neovascularization.

Paragraphs [0284] through [0287] describe the substantial inhibition by squalamine of new blood vessel formation in rabbit corneas.

Although Applicants believe that the above-cited passages from Applicants' specification are more than adequate to teach squlamine as a potent inhibitor of neovascularization, Applicants submit, in order to expedite prosecution of the subject application, a declaration by Kenneth J. Holroyd, M.D., dated April 10, 2002, (and accompanied by Exhibits A to D) which, at the least, concludes that squalamine would be effective in treating neovascularization. This declaration was submitted during prosecution of a parent application, now U.S. Patent 6,962,909. More

specifically, the declaration demonstrates that squalamine was effective in treating two sets of four monkeys whose eyes had been induced with iris neovascularization. In the first test, two of four monkeys that received squalamine exhibited no clinical signs (grade 0) of neovascularization while the other two monkeys treated with squalamine exhibited only a mild form (grade 2) of neovascularization. By comparison, all four monkeys that did not receive squalamine developed severe (grade 4 or 5) neovascularization. In the second test, four of six monkeys, all of which had grade 4 iris neovascularization, were treated with squalamine. After seven days, two of the four treated monkeys showed complete recovery (grade 0) while the other two treated monkeys showed only a mild form (grade 2) of neovascularization. The two monkeys in the test that did not receive squalamine continued to exhibit severe (grade 4) neovascularization.

In pointing out the link between neovascularization and Applicants' claimed treatment of rheumatoid arthritis, paragraph [0247] of Applicants' published application states that the results from the rabbit cornea model (which appears in Applicants' specification and was discussed above) "is indicative in vivo evidence of therapeutic utility in the treatment of pathological disorders of vascularization, including the metastatic spread of tumors, diabetic retinopathy, macular degeneration, and rheumatoid arthritis" (emphasis added). In paragraph [0250], it is even more clearly stated that as "an agent that interferes with the process of neovascularization, squalamine has therapeutic utility in the treatment of diseases or disorders dependent on continued neovascularization where interruption of neovascularization diminishes the intensity of the pathological process. Thus, squalamine has utility for treating disorders including solid tumor growth and metastasis, rheumatoid arthritis, psoriasis, diabetic retinopathy, macular degeneration, neovascular glaucoma, papilloma, retrolental fibroplasia, and organ rejection" (emphasis added).

As further confirmation of the connection between neovascularization (*i.e.*, angiogenesis) and rheumatoid arthritis, Applicants submit herewith for the Examiner's consideration the published journal article "Relationship between angiogenesis and inflammation in experimental arthritis", Eur. Cytokine Netw., 17(3), 202-210 (2006), which concludes that angiogenesis is involved in rheumatoid arthritis.

At least in view of the above-discussed reasons, Applicants submit that claims 26 to 32 are fully supported by the specification. Accordingly, Applicants respectfully request that this rejection be withdrawn.

5. Obviousness Type Double Patenting

Claims 26 to 32 are rejected as allegedly unpatentable over claims 1 to 8 of U.S. Patent No. 5,792,635.

Without acquiescing to the merits of the Examiner's rejection, Applicants file herewith a terminal disclaimer over U.S. Patent No. 5,792,635.

6. Statutory Double Patenting under 35 U.S.C. 101

Claims 26 to 29, 31 and 32 are rejected as allegedly unpatentable over claims 1 to 5 and 14 to 16 of U.S. Patent No. 6,962,909.

Applicants submit that the scope of the claims of the subject application are different from the identified claims of U.S. Patent No. 6,962,909. Applicants point to the test for double patenting under 35 U.S.C. 101, which states that if there is an embodiment of the invention that falls within the scope of one claim but not the other, then statutory double patenting would not exist. Claim 1 of U.S. Patent No. 6,962,909 recites "a method of inhibiting neovascularization in a mammalian eye, comprising administering to the mammal in need thereof a composition comprising an amount of squalamine or a pharmaceutically acceptable salt thereof effective to inhibit the neovascularization." In contrast, claim 26 of the subject application recites a method of treating neovascularization in a mammal, comprising administering to a mammal in need thereof, a composition comprising an amount of squalamine or a pharmaceutically acceptable salt thereof effective to treat the neovascularization. Clearly, there are embodiments of the invention encompassed by claim 26 that are not encompassed by claim 1. Applicants therefore respectfully request that this rejection be withdrawn.

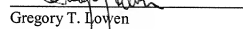
7. Conclusion

The foregoing amendments and remarks are being made to place the application in a condition for allowance. Applicant therefore respectfully requests reconsideration and the timely allowance of the pending claims. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at her convenience.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Dated: **November 19, 2007**
Morgan, Lewis & Bockius LLP
Customer No. **09629**
1111 Pennsylvania Avenue
Washington, D.C. 20004
Tel: 202-739-3000
Fax: 202-739-3001

Respectfully submitted,
Morgan, Lewis & Bockius LLP



Gregory T. Lowen
Registration No. 46,882
Direct: 202-739-5915